

## **REMARKS**

### **Formal Matters**

Claims 1-24 are pending after entry of the amendments set forth herein.

Claims 1-23 were examined. Claims 1-4, 9-12, and 20-23 were rejected.

Claims 1 and 20 have been amended. Support for these amendments is found in the claims as originally filed, as well as in the specification at, for example: Claim 1: paragraph 132 on page 33, paragraph 20 on page 20, paragraph 62 on page 12; and Claim 21: paragraph 93, bridging pages 20 to 21; and paragraph 84, bridging pages 17 to 18.

New Claim 24 has been added. Support for new Claim 24 is found in the claims as originally filed, as well as in the specification at, for example, Claim 1: paragraph 90, page 20.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

No new matter has been added.

### **Entry of Amendment filed July 1, 2004**

Applicants request the entry and consideration of the amendments in the response filed on July 1, 2004, in response to the Office Action dated April 8, 2004.

### **Examiner Interviews**

#### **August 5, 2004**

The undersigned Applicants' representative thanks Examiner Li for the courtesy of a telephonic interview which took place on August 5, 2004, and which was attended by Examiner Li and Applicants' representative Edward J. Baba. During the interview, the rejection of claims 1-4, 9-12, and 20-23 under 35 U.S.C. §112, and §102, was discussed. No agreement was reached during the interview.

#### **September 20, 2004**

The undersigned Applicants' representative thanks Examiner Li and Supervisory Examiner Brumback for the courtesy of a telephonic interview which took place on September 20, 2004, and which was attended by Examiners Li and Brumback and Applicants'

representatives Carol L. Francis and Edward J. Baba. During the interview, the rejection of claims 1-4, 9-12, and 20-23 under 35 U.S.C. §112, and §102, was discussed. The amendments to the claims reflect the discussions, which took place during the interview.

**Rejoinder of Claims 5-8 and 13 indicated as Withdrawn**

Applicants respectfully request that Claims 5-8 and 13 indicated as withdrawn be rejoined with the currently pending claims. These claims are drawn to non-elected species, which species are encompassed by the independent claims from which each of these claims ultimately depends. See MPEP §809.02(B)(b)(2), which states:

(B) When a generic claim is subsequently found to be allowable, and not more than a reasonable number of additional species are claimed, treatment shall be as follows:

(1) When *all* claims to each of the additional species are embraced by an allowable generic claim as provided by 37 CFR 1.141, applicant must be advised of the allowable generic claim and that claims drawn to the nonelected species are no longer withdrawn since they are fully embraced by the allowed generic claim.

Accordingly, Applicants respectfully request that withdrawn claims 5-8 and 13 be reinstated.

**Rejection under 35 U.S.C. §102(b)**

Claims 1-4 and 9-12 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Gether et al., EMBO Journal 16:6737-6747, 1997 (*hereinafter* "Gether et al."). In view of the amendments to the claims and the remarks put forth below, this rejection is respectfully traversed as applied and as it may be applied to the pending claims.

In particular, the Advisory Action maintains the rejection as set forth in the Final Office Action (dated April 8, 2004) and states that "since Gether et al., teaches monitoring conformational changes in a wild type  $\beta$ -2 adrenergic receptor induced by an fluorescent probe, IANDB, attachment to amino acid residues of the conformationally sensitive regions, including 265Cys in the third intracellular loop, the reference of Gether et al. still meets the limitations of the claims" (Advisory Action, page 2).

Without conceding to the correctness of the rejection and in the spirit of expediting prosecution, Claim 1 has been amended to recite a “GPCR **comprising** a conformationally sensitive detectable probe positioned on or within a conformationally sensitive third intracellular domain of the GPCR with the proviso that **no probe is** positioned in a transmembrane domain” as agreed to in the Examiner Interview of September 20, 2004.

In contrast to the presently claimed invention, Gether discloses a series of labeled mutant GPCRs that were produced using the detectable label IANBD (a fluorophore capable of labeling cysteine residues in an apolar environment), which resulted in detectable labeling of cysteines at positions within the third intracellular domain **as well as positions within the transmembrane domain**. Accordingly, Gether et al., does not disclose a GPCR that is labeled with a conformationally detectable probe on the conformationally sensitive third intracellular domain of the GPCR, **without such a probe being also positioned in a transmembrane domain of the receptor**.

The labeled mutant-GPCR disclosed in Gether et al., (Table 1, last line) and noted in the Final Office Action (Page 3, last paragraph) and the Advisory Action, includes a detectable label at position 265, which is in the third intracellular domain. However, the mutant GPCR of Gether et al. **also includes** detectable label at positions 77, 116, and 237, which are all located in the transmembrane domain. Currently, amended Claim 1 recited “**no probe** positioned in a transmembrane domain”. Therefore, the labeled mutant and wild-type GPCRs of Gether et al. are not the GPCR of Claim 1.

Accordingly, since Gether et al. fails to teach each and every element as set forth in the claims, the cited reference fails to anticipate the claimed invention as presented in the Final Office Action (dated April 8, 2004) and the Advisory Action (dated July 26, 2004). Moreover, Gether et al., also fails to teach or suggest labeling of the GPCR on or within the third intracellular domain while not labeling on or within the transmembrane domain. In view of the

above, the Applicants respectfully request that the rejection of claims 1-4 and 9-12 under 35 U.S.C. §102(b) be withdrawn.

**Rejection under 35 U.S.C. §112, second paragraph**

Claims 2 and 20-23 have been rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention, as set out in the Final Office Action. The Advisory Action indicates that the rejection of Claims 2 and 20-23 would be overcome upon entry of the amendments in response to the Final Office Action. Applicants request entry of the amendments as presented in the response to the office action, filed on July 1, 2004. Accordingly, Applicants respectfully request that this rejection be withdrawn.

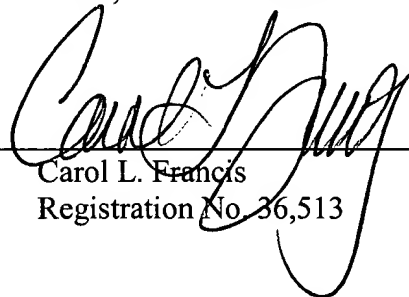
**Conclusion**

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-213.

Respectfully submitted,  
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Date: Oct 7, 2004

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